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Skin activator with glycosaminoglycan production-accelerating effect

Abstract

A skin activator containing as an effective component one or more of the 1-acyl-lysophospholipids represented by the following general formulas (I) and (II), and external skin preparations containing it. It has an excellent glycosaminoglycan production-accelerating effect. ##STR1## wherein R.sup.1 represents a saturated fatty acid residue of 11-18 carbon atoms or a fatty acid residue of 18 carbon atoms and having 1-3 unsaturated double bonds; R.sup.2 represents a saturated fatty acid residue of 13-18 carbon atoms or a fatty acid residue of 18 carbon atoms and having 1-3 unsaturated double bonds; and M represents hydrogen or an alkali metal atom.

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Claims

We claim:

1. A skin activator comprising 0.1 to 10 wt % of one or more 1-acyl-lysophospholipid represented by the following formula ##STR3## wherein R.sup.2 represents a saturated fatty acid residue of 13-18 carbon atoms or a fatty acid residue of 18 carbon atoms and having 1-3 unsaturated double bonds.

2. An external skin preparation comprising a skin activator according to claim 1.

3. An external anti-aging skin preparation comprising a skin activator according to claim 1.

4. A method of increasing the amount of water-retaining glycosaminoglycans in the skin comprising administering to the skin a skin activator according to claim 1 in an amount effective for increasing the amount of water-retaining glycosaminoglycans in the skin.

5. The skin activator according to claim 1, wherein R.sup.2 is an acyl group derived from linolenic acid.

6. The skin activator according to claim 1, wherein R.sup.2 is a soybean-derived fatty acid residue.

7. A cosmetic composition comprising a skin activator according to claim 1.

8. The cosmetic composition according to claim 7 further comprising an inorganic pigment, organic pigment, inorganic powder, organic powder, hydrocarbon, silicone, ester, triglyceride, lanolin, wax, cere, animal or vegetable oil, surfactant, polyhydric alcohol, sugar, vitamin, amino acid, antioxidant, preservative, fragrance, or thickener.

Description

TECHNICAL FIELD

The present invention relates to a skin activator with a glycosaminoglycan production-accelerating effect, containing a 1-acyl-lysophospholipid derivative as an effective component. The skin activator is useful as a cosmetic and an external preparation to prevent skin aging.

BACKGROUND ART

Primary phenomena associated with skin aging include a reduction in "moisture" and "elasticity", and the resulting wrinkles and "sagging". While the causes for this are not yet completely understood, it has been reported in J. Soc. Cosmet. Chem. Japan, 15, 77 (1981), Cell Structure and Function, 9, 357 (1984), Maria, et al., Carbohydrate Research, 159, 127-136 (1987) and elsewhere that one cause is believed to be an age-related decline in the production by skin cells of glycosaminoglycans such as hyaluronic acid, leading to a decrease in the moisture content of the skin which affects skin function. Based on this understanding, and in tandem with methods of forming an oily film on the skin surface for the purpose of passively preventing loss of moisture from the cuticle by perspiration, attention has been focused on the water retention properties of glycosaminoglycans, as a result of which hyaluronic acid derived from cockscombs and Streptococcus bacteria fermentation has been formulated into a variety of cosmetics for supplementation of a hydrophilic component, as a means of preventing wrinkles and "sagging"; however, since the hyaluronic acid in these cosmetics is simply applied onto the skin surface, the macromolecular hyaluronic acid is not absorbed into the skin and thus exhibits only a water-retention effect due to its hygroscopicity. The effect, then, has been lost after washing, resulting in no substantial improvement in skin function. The only disclosed substance which activates skin cell function on the cellular level and enhances the production of glycosaminoglycans as water-retention components is egg enzymolysate, with its fractional components (Japanese Unexamined Patent Publication No. 5-271049).

Simple lysophospholipids, on the other hand, form extremely fine micelles in water due to their single-stranded structure, and thus yield fine emulsions in emulsified systems. They are characterized by having the effect of stabilizing emulsions and preventing starch aging (phenomenon of hardening and emergence due to recrystallization of starch molecules), and are thus used as emulsifiers and as modifiers for bread and the like. According to reports by Uchida, et al. (The Journal of Dermatology, 18, 523-527 (1991)), it has been demonstrated that lysophosphatidylcholine penetrates to the interior of the skin when applied to the skin surface of hairless rats without causing histological damage, and is thus highly safe as a cosmetic. This has led to the development of external skin preparations taking advantage of the safety, low irritancy and stable emulsifying

effect of lysophospholipids (Japanese Unexamined Patent Publication No. 63-41411), but without dealing with their anti-aging effect on skin. Another example is Japanese Unexamined Patent Publication No. 3-161414 wherein lysophosphatidyl glycerol is formulated into a cosmetic for its water-retention effect; however, as in the case where hygroscopic hyaluronic acid is applied onto the skin surface, no effect can be expected once it is washed off.

DISCLOSURE OF THE INVENTION

Based on these results, cell activators which increase the amount of water-retaining glycosaminoglycans in the skin have been found to be effective for activating the skin from the inside, to prevent age-related morphological changes in the skin, typically a reduction in "moisture" and "elasticity" and resulting wrinkles. Nevertheless, it has been desired to develop skin beautifiers with higher glycosaminoglycan-producing ability than the effective components in the skin cosmetics described above. It is, therefore, an object of the present invention to provide a skin activator with a strong glycosaminoglycan production-accelerating effect.

As a result of continuous diligent searching for a glycosaminoglycan production-accelerating substance capable of dealing with the aforementioned problems, the present inventors have discovered that certain lysophospholipids have a notable glycosaminoglycan production-accelerating effect and are highly safe compounds, and upon this basis the present invention has been completed.

In other words, the present invention provides a skin activator containing as an effective component one or more 1-acyl-lysophospholipids represented by the following general formulas (I) and (II): ##STR2## wherein R.sup.1 represents a saturated fatty acid residue of 11-18 carbon atoms or a fatty acid residue of 18 carbon atoms and having 1-3 unsaturated double bonds, R.sup.2 represents a saturated fatty acid residue of 13-18 carbon atoms or a fatty acid residue of 18 carbon atoms and having 1-3 unsaturated double bonds, and M represents hydrogen or an alkali metal atom.

BEST MODE FOR CARRYING OUT THE INVENTION

The 1-acyl-lysophospholipids of the general formulas shown above may be commercially obtained, or they may be obtained by treating commercially available phospholipids with phospholipase A2. Alternatively, a 1-acyl-lysophospholipid with a constant number of carbon atoms may also be obtained by treating synthesized 1,2-diacylphospholipid with phospholipase A2. A compound with a constant carbon chain may also be obtained with a lysophosphatidylcholine obtained by reacting 1 mole or less of a fatty acid anhydride or fatty acid halide with 1 mole of glycerophosphocholine in the presence of a catalyst (Japanese Unexamined Patent Publication No. 63-225388). In addition, a phospholipid derived from soybean or the like may also be treated with phospholipase A2.

In the skin activator of the present invention, when R.sup.1 is a simple acyl group, it is preferably an acyl group derived from oleic acid; when R.sup.2 is a simple acyl group, it is preferably an acyl group derived from linolenic acid; and when R.sup.2 contains 2 or more acyl groups derived from natural substances, it is preferably a soybean-derived fatty acid residue.

The skin activator of the present invention which has a glycosaminoglycan production-accelerating effect may be used as an anti-aging cosmetic for the purpose of preventing wrinkles. To obtain the glycosaminoglycan production-accelerating effect of the invention for the use described above, the mixing ratio of the 1-acyl-lysophospholipid is preferably 0.1 to 10 wt % with respect to the total external skin preparation or formulation. If the amount is less than 0.1 wt %, the desired glycosaminoglycan production acceleration will not be adequately displayed, while if it exceeds much more than 10 wt %, problems such as coloration and odorization of the effective component due to oxidation when an unsaturated fatty acid is present, or stickiness, etc. will result, and thus neither case is practical.

The form of the cosmetic containing the skin activator of the present invention is not particularly limited, and it may contain, in addition to the 1-acyl-lysophospholipid as the effective component, any of a variety of cosmetic components and additives commonly used in cosmetics, including inorganic pigments, organic pigments, inorganic powders, organic powders, hydrocarbons, silicones, esters, triglycerides, lanolins, waxes, cere, animal or vegetable oils, surfactants, polyhydric alcohols, sugars, vitamins, amino acids, antioxidants, preservatives, fragrances, thickeners, and the like.

The present invention is explained in more detail by way of the following examples which, however, are in no way intended to restrict its scope.

EXAMPLES

First, we present the results of experiments conducted to evaluate the effect of the 1-acyl-lysophospholipid

derivatives applied according to the invention.

Evaluation of Glycosaminoglycan Production by NB1RGB Cells

The cells used to evaluate the glycosaminoglycan production acceleration were of the human neonatal dermatofibroblast cell line NB1RGB. This cell line is often conventionally used for such experiments, and was suitable as cells for this experiment. In addition, since human derived cells were used in this experiment, they were even more appropriate as a method of evaluating a drug intended for application to the human body.

NB1RGB cells were densely seeded onto a 1.2 cm-diameter culturing dish (48 wells) at 5.times.10.sup.4 per dish, and cultured for 24 hours at 37.degree. C. in a Dulbecco's modified eagle medium containing 10% fetal calf serum. Each of the 1-acyl-lysophospholipids was then added to Dulbecco's modified eagle medium containing 0.5% fetal calf serum, to a concentration in the medium of 0.5 to 100 .mu.M. After culturing for 24 hours, the cells were transferred to fresh 0.5% calf serum-containing medium to which each of the 1-acyl-lysophospholipids had been added to the same concentration. .sup.3 H-glycosamine was also added to the medium at this time to 370 KBq/ml, and the culturing was continued for another 24 hours. After completion of the culturing, 2 mg pronase in 0.1M Tris.HCl (pH 8) was added, and incubation was performed at 50.degree. C. for one hour. Cetylpyridium chloride was added to a final concentration of 1% in the copresence of 100 .mu.g hyaluronic acid as a carrier, and the resulting precipitate was separated out by centrifuge. The precipitate was centrifuged and washed 3 times in 1 ml of a 1% aqueous cetylpyridium chloride solution, and then 0.2 ml of a 0.05% aqueous cetylpyridium chloride solution containing 0.5M NaCl was added and the mixture was vigorously stirred. To this was then added 5 ml of the emulsification scintillator ACSII, and the radiation was counted with a liquid scintillation counter, making the evaluation based on standard control values. The results, along with the Comparative Examples for contrast, are given in Table 1 below.

TABLE 1

Glycosaminoglycan production (ratio to control)									
	Examples							Comparative Examples	
Concentration	Cmpd 1	Cmpd 2	Cmpd 3	Cmpd 4	Cmpd 5	Cmpd 6	Comp. 1	Comp. 2	
0 .mu.M	1	1	1	1	1	1	1	1	
0.5	1	1	1.2	0.9	1	1			
5	1.1	1.1	1.9	1.1	3	4.7	1	1.2	
10	1.3	1.5		1.9	4	6			
50	3.1	5.6	3		4.2	6			
100	5		2	4.5	5	7	1	1	

Compound 1: Lysophospholipid obtained from soybean phospholipid
Compound 2: Lysophosphatidylcholine obtained from soybean phospholipid
Compound 3: 1linoleyl-lysophosphatidylcholine
Compound 4: 1linolenoyl-lysophosphatidylcholine
Compound 5: 1palmitoyl-lysophosphatidic acid
Compound 6: 1oleoyl-lysophosphatidic acid
Comparison 1: 1decanoyl-lysophosphatidylcholine
Comparison 2: Lysophosphatidyl glycerol

The following are formulation examples of skin activator-containing cosmetics according to the invention.

Example 1 (ointment 1) Parts by weight		
A	1-linolenoyl-lysophosphatidylcholine	1
	White vaseline	25
	Stearyl alcohol	22
B	Propylene glycol	12

Sodium lauryl sulfate	1.5
Preservative/antioxidant	q. s.
Fragrance	q. s.
Purified water	remainder
Total	100

The components listed under A were dissolved in a hot water bath (oil phase), while the components listed under B were separately heated to dissolution (aqueous phase). The aqueous phase was added to and mixed with the oil phase, and after emulsification the mixture was cooled to obtain an ointment.

Example 2 (ointment 2)

		Parts by weight
A	1-oleoyl-lysophosphatidylcholine	2
	White vaseline	40
	Cetanol	18
	Sorbitan sesquioleate	5
	Lauromacrogol	0.5
B	Preservative/antioxidant	q. s.
	Fragrance	q. s.
	Purified water	remainder
	Total	100

The components listed under A were dissolved in a hot water bath (oil phase), while the components listed under B were separately heated to dissolution (aqueous phase). The aqueous phase was added to and mixed with the oil phase, and after emulsification the mixture was cooled to obtain an ointment.

Example 3 (Neutralizing cream)

	Parts by weight
1-linoleoyl-lysophosphatidylcholine	2
Stearyl alcohol	7
Stearic acid	2
Hydrogenated lanolin	2
Squalene	5
2-octyldodecyl alcohol	6
POE (25) cetyl alcohol ester	3
Glycerine monostearate ester	2
Propylene glycol	5
Preservative/antioxidant	q. s.
Fragrance	q. s.
Purified water	remainder
Total	100

The propylene glycol was added to the purified water, heated and kept at 70.degree. C. (aqueous phase). The other components were combined, heated to dissolution and kept at 70.degree. C. (oil phase). The oil phase was added to the aqueous phase, and after pre-emulsification, homogeneous emulsification was performed with a homomixer to obtain a neutralizing cream.

Example 4 (emulsion)		Parts by weight
A	1-linolenoyl-lysophosphatidylcholine	0.5
	Silicone KF56	2
	Isopropyl myristate	3
	POE (20) POP (4) cetyl ether	1
B	Glycerin	3
	Hibiswaco 105	0.2
	Preservative/antioxidant	q.s.
	Fragrance	q.s.
	Purified water	remainder
	Total	100

The above-mentioned formulas A and B were each liquefied at 70.degree. C., A was added to B, and the mixture was homogeneously emulsified to obtain an emulsion.

Example 5 (Skin pack)	Parts by weight
1-acyl-lysophospholipid (soybean)	3
Ethyl alcohol	10
Glycerin	5
Dipropylene glycol	5
Polyethylene glycol 4000	1
Polyvinyl alcohol	10
Vinyl acetate resin emulsion	13
Titanium oxide	12
Olive oil	3
Squalene	0.5
Preservative/antioxidant	q.s.
Fragrance	q.s.
Purified water	remainder
Total	100

The components were uniformly dissolved to obtain a skin pack.

Example 6 (beauty wash)	Parts by weight
1-oleoyl-lysophosphatidic acid	0.5
Glycerine	4
1,3-butylene glycol	4
Ethanol	7
POE (25) oleyl alcohol	0.5
Preservative/antioxidant	q.s.
Fragrance	q.s.
Purified water	remainder
Total	100

The glycerine and 1,3-butylene glycol were dissolved in the purified water. Separately, the 1-oleoyl-lysophosphatidic acid and POE (20) oleyl alcohol were dissolved in the ethanol, and this solution was then added to and dissolved in the previous aqueous solution and filtered to obtain a beauty wash.

INDUSTRIAL APPLICABILITY

As mentioned above, the present invention provides novel and remarkable glycosaminoglycan production-accelerating substances, and skin activating external preparations containing the compounds as effective components thereof display an excellent skin-beautifying effect.

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